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Article type : Original Article

Pre-transplant Social Adaptability Index and clinical outcomes in renal transplantation – The Swiss Transplant Cohort Study

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/CTR.14218

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Disclosures: The authors declare no conflicts of interest.

Funding: The Swiss Transplant Cohort Study is funded by a grant from the Swiss National Research Foundation (Grant number 148512). This work is further supported by unrestricted research grants from Astellas (CH & Europe), Roche (CH) and Novartis (CH).

Data availability statement: Data are available on request from the authors

Abbreviations

CH, Confederatio Helvetica

CHF, Swiss Franc

IQR, InterQuartile Range

HIV, Human Immunodeficiency Virus

HR, Hazard Ratio

NHANES, National Health and Nutrition Examination Survey

PSQ, Psychosocial Questionnaire

SD, Standard Deviation

STCS, Swiss Transplant Cohort Study

US, United States

USD, United States Dollar

Denhaerynck K, Goldfarb-Rumyantzev AS, Sandhu G, Beckmann S, Huynh-Do U, Binet I, De Geest S. Pre-transplant Social Adaptability Index and clinical outcomes in renal transplantation – The Swiss Transplant Cohort Study. Clin Transplant.

Abstract

BACKGROUND: The impact of pre-transplant social determinants of health on post-transplant outcomes remains understudied. In the US, poor clinical outcomes are associated with underprivileged status, as assessed by the Social Adaptability Index (SAI), a composite score of education, employment status, marital status, household income, and substance abuse. Using data from the Swiss Transplant Cohort Study (STCS), we determined the SAI's predictive value regarding two post-transplant outcomes: all-cause mortality and return to dialysis.

METHODS: Between 2012 and 2018, we included adult renal transplant patients (aged ≥18 years) with pre-transplant assessment SAI scores, calculated from a STCS Psychosocial Questionnaire. Time to all-cause mortality and return to dialysis were predicted using Cox regression.

RESULTS: Of 1238 included patients (mean age: 53.8±13.2 years; 37.9% female; median follow-up time: 4.4 years (IQR: 2.7)), 93 (7.5%) died and 57 (4.6%) returned to dialysis. The SAI's hazard ratio was 0.94 (95%CI: 0.88-1.01; p=0.09) for mortality and 0.93 (95%CI: 0.85-1.02; p=0.15) for return to dialysis.

CONCLUSIONS: In contrast to most published studies on social deprivation, analysis of this Swiss sample detected no significant association between SAI score and mortality or return to dialysis.

Keywords: kidney transplantation, socioeconomic factors, mortality, graft survival

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Introduction

Health outcomes result from multilevel, overlapping systems that encompass characteristics not only of individual patients and their social environments, but also of the broader socioeconomic systems within which they reside.[1] Social determinants of health are "the circumstances in which people are born, grow, live, work, and age, and the systems put in place to deal with illness."[2] However, as reported in various healthcare contexts and populations,[2] including organ transplantation,[3-5] differences in those circumstances lead to health disparities, elevating the risks for unfavourable outcomes among socially and/or economically disadvantaged people.[6] Therefore, it may be useful to have pre-transplant indicators that include not only biomedical, but also psychosocial and behavioural risk factors of favourable long-term outcomes. To this end, a comprehensive pre-transplant evaluation has been endorsed by several transplant organizations.[7-10] To support clinicians' pre-transplant evaluations, efforts have also been invested in pre-transplant evaluation instruments.[11-13] In this context, studies of pre-transplant psychosocial and behavioural risk factors or scoring systems are highly relevant, as their findings can increase the rigor of pre-transplant evaluation, which currently includes few pre-transplant social determinants of health.[11-13]

The Social Adaptability Index (SAI), is a US-developed measure of an individual's socio-economic position. It uses a set of risk factors known to influence health outcomes (i.e., educational level, employment status, marital status, household income and substance abuse) to assess the degree to which a patient is (under)privileged.[14-21] A higher SAI score indicates higher social adaptability and has been associated with or shown predictive of better clinical outcomes in both non-transplant[15-17,19,21] and transplant populations—the latter group in terms of graft loss rates,[14,20] mortality,[14] rejection episodes,[20] waiting list times and chances of receiving a transplant.[18] While current evidence suggests that the SAI is predictive of clinical outcomes in the US, its value elsewhere requires substantiation. The implications of being underprivileged may vary between countries depending on their social and healthcare systems. Still, regardless of their location, socially underprivileged persons typically exhibit poorer health behaviour, have less favourable psychosocial profiles and show sub-optimal relationships with their healthcare systems.[6] Representative sampling of the general Swiss population shows associations between socio-economic deprivation and health outcomes such as amenable mortality,[22] breast cancer mortality,[23] systemic inflammation,[24] obesity,[25] frailty,[26] sleep disturbances,[27] lower psychological well-being,[28] and self-reported health,[29,30] mainly attributable to individually measured variables including educational level, income or professional status. Equivalent aggregated (geographically-based) assessments using the same variables show similar results, i.e., higher all-cause mortality, cancers, respiratory and cardiovascular diseases and lower life expectancy, in deprived areas.[31,32]

Despite consensus that transplantation is a chronic health condition that leads to vulnerable long-term health,[33] Switzerland's solid organ transplant recipients have been largely neglected—

certainly in contrast to the general Swiss population—regarding social deprivation and its links with health outcomes. For instance, educational level and household income have been studied as risk factors for, respectively, sleep quality[34] and new-onset obesity.[35] Other studies have named pre-transplant employment status as a predictor of better post-transplant health (with health levels assumed based on post-transplant employment status);[36-38] however, prospective, reliably measured indicators of care deprivation—essential tools to identify the full impact of socioeconomic status on general and transplant-specific long-term health outcomes—are lacking.[33] The measurements of the Swiss Transplant Cohort Study (STCS),[39,40] a nation-wide open cohort study, cover the SAI's variables, along with subsequently assessed outcomes. The current study's main aim was to evaluate whether the SAI predicts post-transplant outcomes *all-cause mortality* and *return to dialysis* up to 7 years post-transplant in adult renal transplant patients.

Materials and methods

Design and sample

From the STCS databank on transplant recipients transplanted in Switzerland's 6 transplant centres, we included all single-graft kidney recipients at least 18 years of age whose files included pre-transplant Psychosocial Questionnaire (PSQ) assessments, and who were recruited between January 2012 and January 2018. Switzerland has a comprehensive health and social security system whereby health insurance is compulsory for all residents. Access to care, including transplantation, is guaranteed. Monthly health insurance premiums average approximately 400 USD per adult, plus co-payments for medication and outpatient care. The government subsidizes persons who cannot afford the cost of premiums. Health indicators for Switzerland are among the best worldwide.[41]

Variables and measurements

Socio-demographic, psychosocial, and behavioural variables were collected pre-transplant (at time of wait-listing) via the PSQ, which employs established instruments and items derived from large population studies (e.g., the Swiss Health Survey, the Swiss HIV cohort study). Comprehensive details of the STCS' design and methods are published elsewhere.[39,40] All-cause mortality and return to dialysis were collected until December 2019.

Social Adaptability Index. As noted above, the SAI is a composite score of five variables: employment status, education level, marital status, substance use (illicit drug use, smoking, alcohol) and household income. After abstracting corresponding PSQ pre-transplant data,[39,40,42] we optimized their fit to the original SAI by weighting each factor according to the original SAI scoring. This was necessary for *marital status* and *substance use* data, as the STCS' PSQ includes neither a 'married with children' category nor an assessment of alcohol use. We used the following scoring: *Employment status*: 0 = unemployed or not working due to medical conditions; 1 = retired; 2 = part-time work/ housewife/man; 3 = full-time work/ education; *Education level*: 0 = mandatory school or less (max. 9 years); 1 = high school graduate/ equivalent; 2 = some college; 3 = college graduate. *Marital status*: 0 = single (i.e., widowed or never married); 1 = divorced or separated; 2 = married or living together; *Substance abuse*: 0 = smoking or illicit drug use within the past year; 1 = either behaviour; 2 = neither behaviour (*Smoking* was assessed by one item from the Swiss HIV Cohort Study,[43] categorized as current, past (stopped < 1y ago), past (stopped > 1y ago), or never. *Household income*: 0 = under 4500 CHF/month, 1 = 4500-6000 CHF/month; 2 = 6001-9000 CHF/month; 3 = over 9000CHF/month. These categories reflect basic living standards in Switzerland.[44]

To enhance inter-study comparability, we scaled the total SAI score (0 – 13, i.e., the sum of the 5 variable scores) to a maximum of 14. A higher score indicates a more favourable social adaptability. The SAI's known-groups validity has been established in the general population, as it distinguishes between groups known to be subject to health disparities.[15] More specifically, it distinguishes regarding gender (higher scores: males), race (higher scores: Caucasian); and geographic location (higher scores: urban) in the general population.

Statistical analysis

Depending on measurement levels and distribution of variables, descriptive statistics, i.e., frequencies, proportions, measures of central tendency (mean, median), measures of dispersion (standard deviation [SD], and interquartile range [IQR]) were calculated as appropriate. To evaluate whether the SAI predicted all-cause mortality and return to dialysis, we performed survival analyses using Cox regression.[45] Analyses were performed in SAS 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical significance was set at $p<0.05$.

Ethical considerations

The STCS was approved by the independent ethics committees of each Swiss transplant centre (EKBB 351/07, KEK 270/07, EKSG 07/122, EK 1487, CER 07-301 [NAC 07-117], Lausanne 284/07). Patients were asked for written informed consent before enrolment. This study was executed in accordance with the ethical principles laid down in the Declaration of Helsinki.

Results

Sample. Of all eligible kidney transplant recipients (n=1446), 91.3% provided informed consent (n=1320), and 1238 (85.6%) had baseline data available. Recipients were on average 53.8 years old (SD 13.2) at the time of transplantation; 37.9% were female (Table 1). The majority of grafts (59.2%) were from deceased donors; 127 recipients had been re-transplanted (13.9%). The median post-transplant follow-up time was 4.4 years (IQR 2.7; range 0.0-7.4). During that period, 93 recipients died (7.5%) and 57 returned to dialysis (4.6%).

Social Adaptability Index. The mean pre-transplant SAI score at transplantation listing was 7.7 (SD 2.9). Regarding the 5 constituent factors, 59.8% of the sample worked part-time or more (or were homemakers); 64.3% were at least high school graduates or equivalent; the majority were married or cohabiting (66.2%); 27.9% reported smoking and/or using illicit drugs; and nearly half (48.7%) had household incomes in the lowest category (i.e., <4500 CHF/month). Exploring associations between patient characteristics and the SAI revealed slightly higher SAI values for recipients who were older, male, Caucasian, had CMV, fewer comorbidities, and shorter dialysis and waiting times. The strongest relationship (R^2=11.6%) was found with graft type: SAI scores were highest for living-unrelated donation (9.4±2.5), followed by living-related donation (8.3±3.0) and deceased donation (7.0±2.6).

Outcome prediction. The hazard ratio of pre-transplant SAI predicting all-cause mortality was 0.94 (95%CI: 0.88-1.01; p=0.085; Table 2) and of return to dialysis 0.93 (95%CI: 0.85-1.02; p=0.148). Analysing SAI subfactors' hazard ratios for both outcomes (Table 2) showed that level of employment predicted mortality; however, the relationship was nonlinear, in that only the category of retired subjects (score=1) was responsible for this lower life expectancy. Controlling for age explained the association between retirement and mortality, suggesting that age, acting as a confounding variable, was the real predictor of mortality for this variable.

Discussion

This prospective study did not demonstrate that the SAI, a measure of (under)privileged status, predicted the post-transplant outcomes of all-cause mortality or return to dialysis in Swiss renal transplant recipients. Compared to most previous research, our hazard ratios indicated lower-end effect sizes[46] (Table 3).[14-21] The SAI has been inversely associated with patient mortality in the general population (as part of NHANES III),[15] chronic kidney disease patients,[17,19] kidney transplant recipients,[14,20] and patients with diabetes.[16] Elsewhere, in patients with end stage renal disease, it has also has also been shown to predict access to wait-listing for renal transplantation and transplantation.[18] In one US sample, the SAI was a strong independent predictor for acute rejection and graft loss but only in African American (vs. non-African American) patients.[20] One study failed to show an association between SAI and depression;[47] another showed nonsignificant results predicting health behavioural and health-related quality of life outcomes in type II diabetics.[21] Our study's exploration of SAI relationships with baseline sample characteristics detected a number of previously-reported associations, such as the association of a higher SAI with shorter waiting times,[18] being of Caucasian descent,[20] having fewer comorbidities,[16,17,19] or having received a living-donor graft compared to one from a deceased donor.[48] While most associations were small (around 1-2% of explained variability), SAI differences were more pronounced between donation types (R^2=12%). Possible explanations are still being investigated.[49]

The SAI has not previously been used in a Western-European context. However, other less granular indices—particularly those assessing social determinants of health in transplantation that are linked to the geographic location of the patient's home[50-52]—found relationships between social deprivation (European Deprivation Index) and survival (but not graft loss) in French kidney transplant recipients,[50] and between mortality and graft loss in English pancreas-kidney transplant recipients (English Index of Multiple Deprivation).[51] Socioeconomically deprived regions in England were also home to more chronic and end-stage kidney disease.[52] In the US as well, neighbourhood social deprivation also correlated with nonadherence to immunosuppressive medications, a determinant of suboptimal long-term outcomes.[53]

Our data were taken from the STCS, a nationwide prospective cohort study including over 95% of patients transplanted in 6 Swiss transplant centers.[39,40] Findings are generalizable for Switzerland, but not necessarily for other countries.[44] Combined with Switzerland's high living standard, its comprehensive health and social insurance system may prevent underprivileged status from acting as an independent risk factor for poor outcomes (e.g., unemployment does not imply losing health insurance). I.e., the small hazard ratios found in this study may be a country-specific effect. On the other hand, in terms of SAI values standardized to a maximum score of 14, our sample's average score of 7.7 positions it solidly in the mid-range of published SAI scores (range: 6.1[47] – 9.2[14]). This may indicate that the SAI lacked the sensitivity to capture existing social deprivation and health inequalities within Switzerland.[54] It needs to be noted that the PSQ's lowest income bracket (<4500 CHF/month; in accordance with Swiss census surveys), is still higher than the official poverty threshold, possibly limiting the income item's sensitivity. In Switzerland, poverty has been associated with incomes under 2293 CHF for a single person and under 3968 CHF for a family with two children.[55]

Another possible reason for our results' divergence from those of previous US research is the difference between American and Swiss socio-economic and regulatory contexts. For instance, access to care, an important driver of outcomes,[56] is never hampered in Switzerland by policies such as restriction of immunosuppressive coverage to the first three years post-transplant.[57] On an individual level, this very likely buffers many of the detrimental health effects of poverty.

Contrary to most global research, paradoxically, Swiss regions with higher income inequality show lower mortality rates.[58] Whether this relates to peculiarities of the Swiss context is unclear. In the US too, geographically-based measures of socio-economic equality have produced associations that depend on the level of aggregation (state vs county),[59] suggesting that hidden causal factors are biasing the apparent associations.[60] Therefore, it would be interesting for future research using STCS data to compare aggregated, geographically-based measures of disparity with their non-aggregated counterparts (e.g., the SAI). This would allow the examination of possible emerging inconsistencies for unknown confounding and/or mediating factors. Also, the possibility remains that with longer follow-up times and a larger STCS sample, the SAI results could become statistically significant; however, this would probably not change the small effect size.

In conclusion, our analysis of data from a sample of Swiss kidney transplant patients resulted in evidence too weak to confirm a link between SAI-measured social deprivation and the clinical outcomes of all-cause mortality and return to dialysis.

Acknowledgments

We thank the transplant patients who participated in the STCS and the STCS staff, who contributed daily to the study's data collection and management. We also thank Chris Shultis for editing this paper.

Authors' specific contributions to the study: SDG, ASGR, GS, and KD participated in research design; SDG, ASGR, GS, SB, UHD, IB, KD & members or the STCS Psychosocial Interest Group participated in writing the paper; SDG & KD, the Psychosocial Interest Group & STCS participated in performance of the research; KD & SDG participated in data analysis.

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Table 1: Sample characteristics (n=1238)

Variable	Measure	Values	SAI higher if…
Demographic and clinical variables			
Age at transplantation in years	Mean ± SD; min-max	53.8±13.2; 18-82	Older ($p=.0008$; $R^2=0.9\%$)
Gender	N (%) females	469 (37.9%)	Male ($p<.0001$; $R^2=1.5\%$)
Ethnicity	N (%) Caucasian	1108 (92.0%)	Caucasian ($p=.0002$; $R^2=1.1\%$)
Cytomegalovirus (CMV)	N (%) Yes	779 (63.4%)	CMV ($p<.0001$; $R^2=1.9\%$)
Co-morbidity categories	N (%) Cancer (except for skin cancer)	141 (14.4%)	Cancer ($p=0.51$; $R^2=0.04\%$)
	N (%) Skin cancer	75 (6.6%)	Skin cancer ($p=0.08$; $R^2=0.3\%$)
	N (%) Cardio-pulmonary diseases (coronary heart disease, peripheral & cerebral vascular diseases, left ventricular dysfunction, pulmonary embolism or venous thrombosis)	613 (54.2%)	No Cardio-pulmonary disease ($p<.0001$; $R^2=1.8\%$)
	N (%) Metabolic, endocrine diseases (diabetes, hyperlipidemia, hypertension)	1022 (91.2%)	Metabolic disease ($p=0.31$; $R^2=0.09\%$)
	N (%) Other events/diseases (e.g., nontransplant surgery, bone fractures, infections, …)	565 (51.1%)	Other event/disease ($p=0.01$; $R^2=0.6\%$)
	Number of co-morbidity categories: Mean ± SD Median; IQR; min-max	2.0±1.1 2; 2; 0-5	Less comorbidities ($p=0.03$; $R^2=0.4\%$)
Time on dialysis (n=816) (in years)	Mean ± SD Median; IQR; min-max	3.3±2.9 3; 3; 0.0-26	Shorter dialysis time ($p<.0001$; $R^2=2.5\%$)
Time on waiting list (in years)	Mean ± SD Median; IQR; min-max	1.6±1.8 0.8; 2.9; 0.0-12.6	Shorter time waiting ($p<.0001$; $R^2=1.7\%$)
Follow up time (in years)	Mean ± SD	4.4±1.7	/

	Median (IQR; min-max)	4.4 (2.7; 0.0-7.4)	
Transplant-related variables			
Graft type	N (%) Living-related donor	237 (19.1%)	Livin-unrelated > -related >
	N (%) Living-unrelated donor	268 (21.7%)	deceased donation (p=.0001;
	N (%) Deceased donor	733 (59.2%)	R^2=11.6%)
Retransplantation	N (%) Re-transplants	172 (13.9%)	No re-tx (p=0.22; R^2=0.1%)
Social Adaptability Index (SAI) variables (pre-transplant)			
SAI (total score)	Mean ± SD	7.7±2.9	
	Median (IQR; min-max)	7.6; 4.2; 0.0-14.0	
Employment	N (%) Unemployed (medically related or not)	318 (25.7%)	
	N (%) Retired	179 (14.5%)	
	N (%) Part time; housewife/-man	468 (37.9%)	
	N (%) Full time; in education	271 (21.9%)	
Education	N (%) Mandatory school or less (max. 9 years)	463 (35.8%)	
	N (%) High school graduate or equivalent	477 (39.2%)	
	N (%) Some college	186 (15.3%)	
	N (%) College graduate	119 (9.8%)	
Marital status	N (%) Single	261 (21.2%)	
	N (%) Divorced/separated	156 (12.7%)	
	N (%) Married/living together	816 (66.2%)	
Substance use	N (%) Illicit drug use and tobacco	31 (2.5%)	
	N (%) Illicit drug use or tobacco	314 (25.4%)	
	N (%) None of the above	890 (72.1%)	
Household income [a]	N (%) < 4500 CHF	493 (48.7%)	
	N (%) 4500-6000 CHF	263 (26.0%)	

	N (%) 6001-9000 CHF	143 (14.1%)
	N (%) > 9000 CHF	113 (11.2%)
Outcome variables (post-transplant)		
All-cause mortality	N (%) of deceased patients	93 (7.5%)
Return to dialysis	N (%) of graft losses	57 (4.6%)

[a] 1 CHF = 0.93€, 1CHF = 1.09 US$; Conversion rates on October 7, 2020; http://www.xe.com/

Table 2: Pre-transplant SAI total and sub-scores as predictors (n=1238)

Variable	Unadjusted Hazard Ratio (95% Confidence Interval)	p-value
SAI total score predicting *all cause mortality*		
All cause mortality	0.94 (0.88-1.01)	0.085
SAI total score predicting *return to dialysis*		
Return to dialysis	0.93 (0.85-1.02)	0.148
SAI-components: 5 separate models predicting *all cause mortality*		
Employment	0.75 (0.62-0.90)	0.002
Education	1.04 (0.84-1.29)	0.717
Household income	0.87 (0.70-1.09)	0.238
Marital status	0.98 (0.83-1.16)	0.821
Substance use	0.88 (0.69-1.13)	0.328
SAI-components: 5 separate models predicting *return to dialysis*		
Employment	0.87 (0.69-1.10)	0.258
Education	0.76 (0.56-1.04)	0.085
Household income	0.90 (0.67-1.20)	0.459
Marital status	0.95 (0.77-1.17)	0.620
Substance use	0.97 (0.70-1.36)	0.875

Table 3: Overview of studies using the SAI

Study	**Population**	**Mean ± standard deviation**	**Outcome**	**Hazards ratio / Means ± standard deviation / R² & p-values**	**Cohen's d**
This study	Kidney transplants (CH)	7.7±2.6	Mortality	HR 0.94 (0.88 – 1.01), p=0.085	-0.037 (-0.077 – 0.006)
			Graft loss	HR 0.93 (0.85 – 1.02), p=0.148	-0.032 (-0.071 – 0.009)
Goldfarb et al. 2011[18]	Kidney transplants (US)	7.1±2.5	Wait listed	HR 1.19 (1.15 – 1.23), p < .001	0.104 (0.084 – 0.124)
			Receiving transplant	HR 1.06 (1.03 – 1.09), p < .001	0.035 (0.018 – 0.052)
Goldfarb et al. 2010[17]	ESRD (US)	7.3±2.7	Mortality	HR 0.88 (0.86 – 0.89), p < .001	-0.077 (-0.091 – -0.070)
Sandhu et al. 2011[19]	Dialysis (US)	7.1±2.5	Mortality	HR 0.97 (0.95 – 0.99), p = .006	-0.018 (-0.031 – -0.006)
Goldfarb et al. 2011[15]	General population (US)	8.3	Mortality	HR 0.87 (0.84 – 0.90), p < .001	-0.084 (-0.105 – -0.063)
Goldfarb et al. 2012[16]	Diabetes (US)	6.6±2.4	Mortality	HR 0.90, p < .001	-0.063
Garg et al. 2012[14]	Kidney transplants (US)	9.2±2.5	Graft loss	HR 0.89, p < .05	-0.070
			Mortality	HR 0.84, p < .01	-0.105
Santos 2013[30]	Depressed patients (Brazil)	6.1±1.8	Being depressed	6.1±1.6 vs. 6.2±1.9, p=0.901	-0.05 (-0.31 – 0.41)
Taber 2016[20]	Kidney transplants (US)		Acute rejection		
	-African Americans	6.5	-African Americans	HR 0.89 (0.80 – 0.99), p < .027	-0.070 (-0.134 – -0.006)
	-Non-African Americans	7.8	-Non-African Americans	HR 0.92 (0.81 – 1.05), p < .215	-0.050 (-0.127 – 0.029)
			Graft loss		
			-African Americans	HR 0.23 (0.06 – 0.93), p < .039	-0.882 (-0.689 – -0.044)
			-Non-African Americans	HR 1.01 (0.28 – 3.62), p < .993	0.006 (-0.764 – 0.772)
Campbell 2017[21]	Diabetes patients (US)		General diet	R^2=0.0016, NS	0.003
			Specific diet	R^2=0.0063, NS	0.01
			Exercise	R^2=0.0004, NS	0.001

	Blood sugar	R^2=0.0008, NS	-0.001
	Foot care	R^2=0.0013, NS	-0.002
	A1c	R^2=0.0008, NS	-0.002
	Blood pressure	R^2=0.0015, NS	0.003
	Lipids	R^2=0.0001, NS	-0.0002
	Health-related quality of life		
	- Physical component	R^2=0.0002, NS	0.0004
	- Mental component	R^2=0.23, p<.001	0.67